UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/529,715	04/19/2000	MAMORU OHASHI	2000-0486A	9675

7590 06/09/2003

WENDEROTH LIND & PONACK
2033 K STREET NW
SUITE 800
WASHINGTON, DC 20006

EXAMINER
GOLLAMUDI, SHARMILA S

ART UNIT	PAPER NUMBER
1616	18

DATE MAILED: 06/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/529,715	Applicant(s) OHASHI ET AL.	
	Examiner Sharmila S. Gollamudi	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20 and 61-88* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20 and 61-88* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Receipt of Extension of Time, Amendment D, and Rule 132 Declaration received on April 4, 2003 is acknowledged. Claims 1-20 and 61-88 are pending in the prosecution of this application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-20 and 63-88 are rejected under 35 U.S.C. 103(a) as being unpatentable over Negoro et al (5,258,382) in view of Muller et al (5,858,410).

Negoro et al teach the instantly claimed aldose reductase inhibitor compound in a pharmaceutical composition for the treatment of diabetes (see abstract). The reference discloses the aldose reductase inhibitor in fine granules (1%) with a diluent (73%), a binder (3%), a lubricant (1%), and disintegrator (22%) (See example 29).

Negoro et al does not specify the particle size of the active or the dissolution rate.

Muller et al teach pharmaceutical compositions containing an active that is insoluble or sparingly soluble. Muller discloses that the dissolution rate increases as the particles surface area increases in accordance with the Noyes-Whitney law. As a results of increased dissolution rate increases bioavailability (col. 1, lines 44-50). Muller discloses a marked increase in saturation solubility and in turn dissolution with the reduction of particle diameter and increased surface area from microns to nanometers

(col.5, lines 58-60 and col. 7, lines 7-10). The reference teaches a particle in the range of 10 to 1,000 nm and 65% dissolution rate within ten minutes (col. 2, lines 40, col. 14, lines 49-55 and figures).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to reduce the particle size of the active to less than 20 microns since Muller et al disclose that increased surface area through reduction of particle size allows a faster rate of dissolution. One would be motivated to do so with the expectation of similar results since Muller teaches a sparingly soluble or insoluble drug and the instant active agent is also sparingly soluble.

Response to Arguments

Applicant argues that the instant invention is a pharmaceutical composition comprising an active ingredient micronized particles having a mean particle size less than about 20 microns, preferably less than about 10 microns, and particularly about 0.5 to 3 microns in a specific ratio of additives. It is argued that these features provide excellent dissolving properties. It is argued that Muller et al teach 10 to 1,000 nm for increased dissolution, which is too small for the instant invention. Secondly, the applicant argues that the amendment distinguishing instant invention as a solid dosage form, distinguishes it from Muller's suspension. Applicant argues that Muller et al utilizes a different dissolution method than the instant Paddle method. Applicant submits several brief summaries of publication discussing the theory of particle dissolution.

In regards to the prior art arguments, the examiner points out that the claim 1 only recites a particle size of less than 20 microns. As recognized by the applicant,

Muller et al clearly teach a range of 10 nm to 1,000 corresponding to 0.01 to 1 microns, which that falls within the instant range. Newly submitted claims 83-85 also overlap the prior art's particle range. Additionally, claims 86-88 merely recite "above 1 micron" which does not distinguish over the prior art since Muller teaches 1 micron and less. The question is how much above 1 micron? For instance, 1.001 is above 1 micron but it is still would be obvious to one of ordinary skill in the art thorough routine optimization. In regards to the unexpected results, the applicant lowest range is 1.5 microns. Furthermore, although the applicant argues that the range taught by Muller is too small, the claims do not reflect this argument since clearly Muller's range is included in claimed range. Claims 5 and 13 recite particular ratios without the particle sizes, the examiner points out that these ratios are taught by the primary reference Negoro et al.

In regards to the different dissolution methods utilized, the examiner points out that the examiner relies on the basic theory of Noyes-Whitney law therefore, the theory would be the same regardless of the type of dissolution method used. Furthermore in regards to the solid dosage form, this does not overcome the rejection since the primary reference teaches solid dosage forms. The examiner relies on Muller solely for the dissolution theory and not the pharmaceutical composition. The Noyes Whitney law is in regards to the dissolution of solid particles.

Lastly in regards to the publications, the examiner notes that reduced particle size causes problems and that according one publication submitted, that the size should be that of the submicron level. However, the examiner points out that the instant claims recite the submicron levels.

Response to Amendment

The Declaration under 37 CFR 1.132 filed April 4, 2003 is insufficient to overcome the rejection of claim1-20 and 63-88 based upon obviousness as set forth in the last Office action because: First, the claims are not commensurate in scope with the claims. The declaration provides for the lower limit of 1.5 microns, which is not recited in the claims. Secondly, the examiner points out that the unexpected results are very expected according to the Noyes-Whitney law that predicts that the larger the specific surface area of the drug substance, the faster the dissolution rate. The applicant's results indicate that 87 micron particles dissolve the slowest, then the 10 micron particles, with 1.5 micron particles having the fastest dissolution. Therefore, the applicant has not overcome the secondary reference. Furthermore, applicant is arguing against the Muller reference and yet has not provided unexpected results with the relevant art. Lastly, the examiner points out that claims 5 and 13 do not recite particles sizes, therefore the Declaration cannot overcome the rejection of these two claims since Negoro also teaches the same additive ratios.

Claims 61-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Negoro et al (5,258,382) in view of Muller et al (5,858,410) in further view of Schneider et al (5,356,636).

As set forth above, Negoro et al teach the instant active and Muller et al teach the instant particle sizes to increase dissolution. Muller et al teach the use of stabilizers to cover the surface of the particles to prevent aggregation (col. 7).

The references do not teach the instant acids in the composition.

Schneider et al teach the instant acids as stabilizers (col. 4, lines 68) in compositions.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add the instant acids since Schneider et al teach these acids as stabilizers for the actives.

Response to Arguments

Applicant argues that Schneider teaches utilizing the instant acids for preventing oxidation and only phytic acid is exemplified.

Applicant's arguments have been fully considered but they are not persuasive. The examiner points out that in an obviousness type rejection the prior art need not exemplify the instant components, it merely needs to suggest the use of them. The reference teaches antioxidants for the prevention of oxidation of the active and the instant acids as stabilizers as clearly seen on column 4, line 68. Applicant has incorrectly interpreted the passage. The applicant's uses the instant acids as stabilizers as seen on page 6 of instant specification. Furthermore, regardless of how the acid accomplishes the stabilization of the composition, it still stabilizes the composition.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is (703) 305-2147. The examiner can normally be reached on M-F (7:30-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose Dees can be reached on (703) 308-4628. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SSG

June 3, 2003

MICHAEL G. HARTLEY
PRIMARY EXAMINER